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FORM PTO-1449 <u>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</u>			ATTY. DOCKET NO. 1735.0470001/RWE/ALS	APPLICATION NO. 09/920,332			
			APPLICANT Kasibhatla, S. et al.				
			FILING DATE 08/02/01	GROUP 1644			
U. S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	RELINQUISH DATE
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
AL							Yes No
AM							Yes No
AN							Yes No
AO							Yes No
<i>PJK</i>	AP2	WO 01/79187 A2	10/25/01	WIPO			Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR						
	AS						
<i>PJK</i>	AT	14	Biomol. Research Laboratories, Inc., "Apoptosis Inducers and the Assay of Caspase Activity," FASEB J. 12:A1488, Abstract No. T10, Federation of American Societies for Experimental Biology (1998).				
EXAMINER <i>PJK</i>					DATE CONSIDERED 7/30/03		
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FILING DATE
08/02/01

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U.S. PATENT DOCUMENTS

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PNT	AL3	WO 02/12545 A2	2/14/02	WIPO			Yes No
	AM3						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PNT	AR	15	Hug, H. et al., "Rhodamine 110-Linked Amino Acids and Peptides as Substrates to Measure Caspase Activity upon Apoptosis Induction in Intact Cells," <i>Biochem.</i> 38: 13906-13911, American Chemical Society (October 1999).
	AS	15	Jones, J. et al., "Development and Application of a GFP-FRET Intracellular Caspase Assay for Drug Screening," <i>J. Biomol. Screening</i> 5:307-317, The Society for Biomolecular Screening (October 2000).
↓	AT	15	Leoni, L.M. et al., "Indanocine, a Microtubule-Binding Indanone and a Selective Inducer of Apoptosis in Multidrug-Resistant Cancer Cells," <i>J. Natl. Canc. Inst.</i> 92:217-224, Oxford University Press (February 2000)..

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	AO						Yes No
	AP						Yes No

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<i>Pnkt</i>	AR	<u>16</u>	Monks, A. et al., "Feasibility of a High-Flux Anticancer Drug Screen Using a Diverse Panel of Cultured Human Tumor Cell Lines," <i>J. Natl. Canc. Inst.</i> 83:757-766, Oxford University Press (1991).
	AS	<u>16</u>	Mooberry, S.L. et al., "Laulimalide and Isolaulimalide, New Paclitaxel-Like Microtubule-Stabilizing Agents," <i>Canc. Res.</i> 59:653-660, American Society for Cancer Research (February 1999).
↓	AT	<u>16</u>	Tepper, A. D. et al., "CD95/Fas-induced Ceramide Formation Proceeds with Slow Kinetics and is not Blocked by Caspase-3/CPP32 Inhibition," <i>J. Biol. Chem.</i> 272: 24308-24312, The American Society for Biochemistry and Molecular Biology, Inc., (1997).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>PNK</i>	AR	<u>17</u>	Zhou, T. et al., "Bisindolylmaleimide VIII facilitates Fas-mediated apoptosis and inhibits T cell-mediated autoimmune diseases," Nat. Med. 5:42-48, Nature Publishing Company (January 1999).
	AS	<u>17</u>	International Search Report for International Application No. PCT/US01/24250 (published as document AM3), mailed May 31, 2002.
	AT	<u>17</u>	Co-pending U.S. Patent Application No. 10/046,548, Kasibhatla, S. et al., filed January 16, 2002.

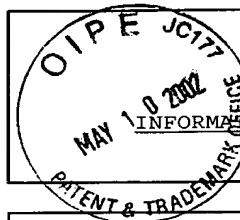
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		ATTY. DOCKET NO. 1735.0470001/RWE/ALS		APPLICATION NO. 09/920,332	
		APPLICANT Kasibhatla et al.			
		FILING DATE August 2, 2001		GROUP 1644	

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
PNK	AA1	4,336,186	06/22/1982	Gargiulo et al.	260	112.5 R	02/09/1981
	AB1	4,557,862	12/10/1985	Mangel et al.	260	112 R	10/28/1983
	AC1	4,640,893	02/03/1987	Mangel et al.	435	23	09/27/1985
	AD1	5,208,148	05/04/1993	Haugland et al.	435	14	12/07/1990
	AE1	5,227,487	07/13/1993	Haugland et al.	546	15	04/16/1990
	AF1	5,362,628	11/08/1994	Haugland et al.	435	18	03/05/1993
	AG1	5,443,986	08/22/1995	Haughland et al.	435	4	07/06/1993
	AH1	5,556,992	09/17/1996	Gaboury et al.	549	227	09/02/1994
	AI1	5,576,424	11/19/1996	Mao et al.	536	17.9	11/08/1994
	AJ1	5,587,490	12/24/1996	Goodrich, Jr., et al.	549	282	12/10/1993
↓	AK1	5,605,809	02/25/1997	Komoriya et al.	435	23	10/28/1994

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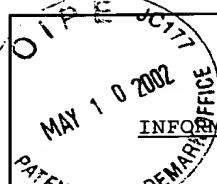
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
PNK	AL1	WO 93/10461	05/27/1993	WIPO			RECEIVED Yes
	AM1	EP 0 285 179 B1	06/16/1993	Europe			RECEIVED MAY 13 2002 Yes
	AN1	CA 2,119,840	09/27/1994	Canada			RECEIVED TECH CENTER 1600/2900 Yes
	AO1	WO 96/20721	07/11/1996	WIPO			RECEIVED 1600/2900 No
↓	AP1	WO 98/57664	12/23/1998	WIPO			RECEIVED Yes
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PNK	AR	1	Assfalg-Machleidt, I., et al., "Membrane Permeable Fluorogenic Rhodamine Substrates for Selective Determination of Cathepsin L," <i>Biol. Chem. Hoppe-Seyler</i> 373:433-440, Walter de Gruyter & Co. (1992).
↓	AS	1	Bonneau, P., et al., "Design of Fluorogenic Peptide Substrates for Human Cytomegalovirus Protease Based on Structure-Activity Relationship Studies," <i>Anal. Biochem.</i> 255:59-65, Academic Press, Inc. (1998).
↓	AT	1	DiIanni, C.L., et al., "In Vitro Activity of the Herpes Simplex Virus Type 1 Protease with Peptide Substrates," <i>J. Biol. Chem.</i> 268:25449-25454, American Society for Biochemistry and Molecular Biology, Inc. (1993).

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	APPLICANT Kasibhatla et al.	
	FILING DATE August 2, 2001	GROUP 1645 1644

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
PSK	AA2	5,698,411	12/16/1997	Lucas et al.	435	29	05/18/1995
	AB2	5,714,342	02/03/1998	Komoriya et al.	435	23	10/27/1995
	AC2	5,733,719	03/31/1998	Jaffe et al.	435	4	05/18/1995
	AD2	5,773,236	06/30/1998	Diwu et al.	435	15	04/25/1997
	AE2	5,776,720	07/07/1998	Jaffe et al.	435	29	05/18/1995
	AF2	5,834,216	11/10/1998	Roizman et al.	435	7.21	09/06/1995
	AG2	5,843,635	12/01/1998	Schlossman et al.	435	5	02/27/1995
	AH2	5,849,513	12/15/1998	Jaffe et al.	435	29	07/31/1997
	AI2	5,871,946	02/16/1999	Lucas et al.	435	18	05/18/1995
	AJ2	5,897,992	04/27/1999	Fearnhead et al.	435	29	09/27/1996
	AK2	5,908,750	06/01/1999	Reed, J.C. et al.	435	6	04/11/1997

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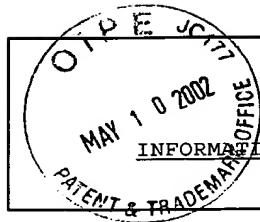
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
PSK	AL2	WO 99/18856	04/22/1999	WIPO			RECEIVED Yes No
	AM2	WO 00/07017	02/10/2000	WIPO			MAY 7, 2002 Yes No
	AN2	WO 00/45165	08/03/2000	WIPO			TECH CENTER 1600/2000 Yes No
	AO2	WO 98/55863	06/05/1998	WIPO			1600/2000 Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PSK	AR	2	Dinarello, C.A., "Interleukin-1 and Interleukin-1 Antagonism," <i>Blood</i> 77:1627-1652, The American Society of Hematology (1991).
	AS	2	Friesen, C., et al., "Involvement of the CD95 (APO-1/Fas) receptor/ligand system in drug-induced apoptosis in leukemia cells," <i>Nat. Med.</i> 2:574-577, Nature Publishing Group (1996).
	AT	2	Fulda, S., et al., "Betulinic Acid Triggers CD95 (APO-1/FAS)- and p53-independent Apoptosis via Activation of Caspases in Neuroectodermal Tumors," <i>Canc. Res.</i> 57:4956-4964, American Association for Cancer Research (1997).

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August 2, 2001

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
PSH	AA3	5,976,822	11/02/1999	Landrum et al.	435	23	08/20/1997
	AB3	6,075,020	06/13/2000	Cincotta et al.	514	224.8	12/03/1998
	AC3	6,077,684	06/20/2000	Kravtsov	435	30	11/14/1996
	AD3	6,200,969 B1	03/13/2001	Fritz et al.	514	214	09/12/1997
	AE3	6,248,904 B1	06/19/2001	Zhang et al.	549	227	07/21/1999
	AF3	6,251,614 B1	06/26/2001	Fritz et al.	435	7.2	05/10/1999
	AG3	6,270,980 B1	08/07/2001	Fritz et al.	435	7.3	06/05/1997
	AH3	6,335,429 B1	01/01/2002	Cai et al.	530	402	03/08/2000
	AI3	6,342,611 B1	01/29/2002	Weber et al.	549	227	10/09/1998
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						RECEIVED Yes No
	AM						RECEIVED Yes No
	AN						RECEIVED MAY 13 2002 Yes No
	AO						RECEIVED TECH CENTER 1600/2900 Yes No
	AP						RECEIVED Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PSH	AR	3	Gallop, M.A., et al., "Applications of Combinatorial Technologies to Drug Discovery. 1. Background and Peptide Combinatorial Libraries," <i>J. Med. Chem.</i> 37:1233-1251, American Chemical Society (1994).
	AS	3	Gamen, S., et al., "Doxorubicin-induced apoptosis in human T-cell leukemia is mediated by caspase-3 activation in a Fas-independent way," <i>FEBS Lett.</i> 417:360-364, Elsevier Science B.V. (1997).
	AT	3	Ganesh, S., et al., "Flow Cytometric Determination of Aminopeptidase Activities in Viable Cells Using Fluorogenic Rhodamine 110 Substrates," <i>Cytometry</i> 20:334-340, Wiley-Liss, Inc. (1995).

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	AM						Yes No
	AN						MAY 18 2002 RECEIVED Yes No
	AO						TECH CENTER 1600/2900 Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PNK	AR	4	Gordon, E.M., et al., "Applications of Combinatorial Technologies to Drug Discovery. 2. Combinatorial Organic Synthesis, Library Screening Strategies, and Future Directions," <i>J. Med. Chem.</i> 37:1385-1401, American Chemical Society (1994).
↓	AS	4	Hardin, J.A., et al., "A simple fluorescence method for surface antigen phenotyping of lymphocytes undergoing DNA fragmentation," <i>J. Immunol. Meth.</i> 154:99-107, Elsevier Science Publishers B.V. (1992).
↓	AT	4	Haugland, R.P. and Johnson, I.D., "Detecting Enzymes in Living Cells Using Fluorogenic Substrates," <i>J. Fluorescence</i> 3:119-127, Plenum Publishing Corporation (1993).

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AM						MAY 1, 2002 Yes No
AN						TECH CENTER 1600/2000 Yes No
AO						Yes No
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PNK	AR	5	Haugland, R.P., "Detecting Enzymatic Activity in Cells Using Fluorogenic Substrates," <i>Biotechnic & Histochemistry</i> 70:243-251, Williams & Wilkins (1995).
	AS	5	Haugland, R.P., <i>Handbook of Fluorescent Probes and Research Chemicals</i> , 6 th Ed., Spence, M.T.Z., ed., Molecular Probes, Inc., Eugene, Oregon, pp. 28, 54, 225-234 (1996).
↓	AT	5	Hickman, J.A., "Apoptosis induced by anticancer drugs," <i>Cancer Metastasis Rev.</i> 11:121-139, Kluwer Academic Publishers (1992).

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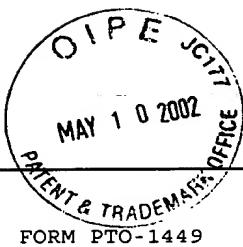
PNK	AR	6	Holskin, B.P., et al., "A Continuous Fluorescence-Based Assay of Human Cytomegalovirus Protease Using a Peptide Substrate," <i>Anal. Biochem.</i> 226:148-155, Academic Press, Inc. (1995).
	AS	6	Johnson, A.F., et al., "Nonisotopic DNA Detection System Employing Elastase and a Fluorogenic Rhodamine Substrate," <i>Anal. Chem.</i> 65:2352-2359, American Chemical Society (1993).
↓	AT	6	Klingel, S., et al., "Flow Cytometric Determination of Cysteine and Serine Proteinase Activities in Living Cells with Rhodamine 110 Substrates," <i>Meth. Cell Biol.</i> 41:449-459, Academic Press, Inc. (1994).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PSH	AR	7	Leytus, S.P., et al., "New class of sensitive and selective fluorogenic substrates for serine proteinases," Biochem. J. 215:253-260, The Biochemical Society (1983).
	AS	7	Leytus, S.P., et al., "Rhodamine-based compounds as fluorogenic substrates for serine proteinases," Biochem. J. 209:299-307, The Biochemical Society (1983).
↓	AT	7	Los, M., et al., "Requirement of an ICE/CED-3 protease for Fas/APO-1-mediated apoptosis," Nature 375:81-83, Nature Publishing Group (1995).

EXAMINER	<i>PL W 5/22</i>	DATE CONSIDERED	<i>7/30/03</i>
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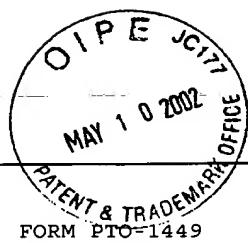
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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

PSK	AR	8	Los, M., et al., "Cross-Resistance of CD95- and Drug-Induced Apoptosis as a Consequence of Deficient Activation of Caspases (ICE/Ced-3 Proteases)," <i>Blood</i> 90:3118-3129, American Society of Hematology (1997).
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EXAMINER	<i>JL N S</i>	DATE CONSIDERED	<i>1/30/03</i>
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.			



PATENT & TRADEMARK OFFICE FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1735.0470001/RWE/ALS	APPLICATION NO. 09/920,332
	APPLICANT Kasibhatla et al.	
	FILING DATE August 2, 2001	GROUP 1645 1644

U. S. PATENT DOCUMENTS

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
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<i>PNK</i>	AR	9	Molecular Probes, Inc., "Alphabetical Price List of New Products January 1994," Molecular Probes, Inc., Eugene, Oregon, pp. 1-4 (1994).
	AS	9	Morliere, P., et al., "Interaction of Tetrapyrrolic Rings with Rhodamine 110 and 123 and with Rhodamine 110 Derivatives Bearing A Peptidic Side Chain," <i>Biochem. Biophys. Res. Comm.</i> 146:107-113, Academic Press, Inc. (1987).
<i>↓</i>	AT	9	O'Boyle, D.R., et al., "Identification of a Novel Peptide Substrate of HSV-1 Protease Using Substrate Phage Display," <i>Virology</i> 236:338-347, Academic Press, Inc. (1997).

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>		ATTY. DOCKET NO. 1735-0470001/RWE/ALS	APPLICATION NO. 09/920,332
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
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	AN						Yes No
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<i>PNK</i>	AR	<u>10</u>	Qi, X.-M., et al., "Baculovirus p35 and Z-VAD-fmk inhibit thapsigargin-induced apoptosis of breast cancer cells," <i>Oncogene</i> 15:1207-1212, Stockton Press (1997).
	AS	<u>10</u>	Richards, A.D., et al., "Sensitive, Soluble Chromogenic Substrates for HIV-1 Proteinase," <i>J. Biol. Chem.</i> 265:7733-7736, American Society for Biochemistry and Molecular Biology, Inc. (1990).
	AT	<u>10</u>	Rothe, G., et al., "Flow Cytometric Analysis of Protease Activities in Vital Cells," <i>Biol. Hoppe-Seyler</i> 373:547-554, Walter de Gruyter & Co. (1992).

EXAMINER	<i>J. S.</i>	DATE CONSIDERED	<i>7/30/03</i>
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	AL					Yes No
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PWT	AR	<u>11</u>	Stevens, J.T., et al., "In vitro proteolytic activity and active-site identification of the human cytomegalovirus protease," <i>Eur. J. Biochem.</i> 226:361-367, Springer International (1994).
	AS	<u>11</u>	Tamburini, P.P., et al., "A Fluorometric Assay for HIV-Protease Activity Using High-Performance Liquid Chromatography," <i>Anal. Biochem.</i> 186:363-368, Academic Press, Inc. (1990).
↓	AT	<u>11</u>	Thornberry, N.A., et al., "A Combinatorial Approach Defines Specificities of Members of the Caspase Family and Granzyme B," <i>J. Biol. Chem.</i> 272:17907-17911, The American Society for Biochemistry and Molecular Biology, Inc. (1997).

EXAMINER <i>Spencer S. Krueger</i>	DATE CONSIDERED <i>7/20/03</i>
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		APPLICANT Kasibhatla et al.	
		FILING DATE August 2, 2001	GROUP <u>1645</u> 1644

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	AL					Yes No
	AM					Yes No
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PWK	AR	<u>12</u>	Thornberry, N.A., "Caspases: key mediators of apoptosis," <i>Chem. Biol.</i> 5:R97-R103, Current Biology Ltd. (1998).
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↓	AT	<u>12</u>	Tyagi, S.C. and Carter, C.A., "Continuous Assay of the Hydrolytic Activity of Human Immunodeficiency Virus-1 Protease," <i>Anal. Biochem.</i> 200:143-148, Academic Press, Inc. (1992).

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	AL						Yes No
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<i>PJK</i>	AR	<u>13</u>	Weber, J.M., "Adenovirus Endopeptidase and Its Role in Virus Infection," in: The Molecular Repertoire of Adenoviruses I. Virion Structure and Infection, Doerfler, W. and Böhm, P., eds., Springer-Verlag, Berlin, Germany, pp.227-235 (1995).
	AS	<u>13</u>	Zhang, R., et al., "Probing the Substrate Specificity of Hepatitis C Virus NS3 Serine Protease by Using Synthetic Peptides," J. Virol. 71:6208-6213, American Society for Microbiology (1997).
<i>↓</i>	AT	<u>13</u>	International Search Report for International Application No. PCT/US00/02329 (published as document AM3), mailed May 10, 2000.

EXAMINER <i>J. N. S.</i>	DATE CONSIDERED <i>7/31/00</i>
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		APPLICANT Kasibhatla et al.	
		FILING DATE August 2, 2001	GROUP 1645 <i>1644</i>

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>PNK</i>	AR	<u>14</u>	Co-pending U.S. Application No. 09/454,595, Weber, E. et al., filed December 7, 1999.
<i>PNK</i>	AS	<u>14</u>	Allen, R.T., et al., "Mechanisms controlling cellular suicide: role of Bcl-2 and caspases," Cell. Mol. Life Sci. 54:427-445, Birkhäuser Verlag (1998).
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EXAMINER <i>Jlyn S</i>	DATE CONSIDERED <i>7/30/03</i>
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